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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,478	02/19/2002	L. Curtis Hannah	UF-178AXC2	7981

23557 7590 08/08/2003

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
2421 N.W. 41ST STREET
SUITE A-1
GAINESVILLE, FL 326066669

EXAMINER	
KUBELIK, ANNE R	
ART UNIT	PAPER NUMBER
1638	9

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/079,478	HANNAH ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-26 and 29-41* is/are pending in the application.

4a) Of the above claim(s) *4,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-26 and 29-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group I (claims 1, 3, 5-8, 10-26 and 30-41) in Paper No. 8, filed 9 May 2003, is acknowledged. Claim 9 should have been in Group I, rather than Group II, and claim 29 should be in Group I, rather than group V; thus, these claims will thus be examined along with claims 1, 3, 5-8, 10-26 and 30-41. Claims 4 and 27-28 are withdrawn from consideration as being drawn to nonelected inventions.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from either the legends or the Brief Description of Figures 2-5.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

3. Applicant's claiming of priority to Provisional Applications 60,085,460, filed 14 May 1998, and 60/031,045 filed 18 November 1996, are improper because these applications were filed more than one year before the filing date of the instant application, 19 February 2002. It is Application 09/312,433 that claims priority to 60,085,460, and Application 08/972,545 that claims priority to 60/031,045. Correction is required.

Claim Objections

4. Claims 11-13, 16, 19, 22, 25, 34-36, 38 and 41 are objected to because of the following informalities:

In claims 11-13 and 34-36 an article is missing before "wild-type" in line 3 and a comma should be inserted after "enzyme" in line 2.

In claims 16, 22 and 38, "lilies" should be singular to be consistent with "monocotyledonous plant".

In claims 19, 25 and 41, "peas" and "trees" should be singular to be consistent with "dicotyledonous plant".

5. Claims 30-36 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 5-8 and 11-13. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Alternately, see the 35 USC 112, 2nd rejection below.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1, 3, 5-9, 10-13, 20-26 and 30-41 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a polynucleotide or to a plant, which read on a product of nature.

The DNA molecule and the plant, as claimed, have the same characteristics and utility as naturally occurring mutants and therefore does not constitute patentable subject matter. In the absence of

the hand of man, the naturally occurring products are considered non-statutory subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claims be modified to refer to the hand of the inventor, *e.g.* by replacement of "A" in claim 1 with --An isolated-- or --A purified-- and to indicate in claim 20 that the polynucleotide is comprised within a construct. See MPEP 2105.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 3, 5-26 and 29-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain polynucleotides that encode heat stable ADP-glucose pyrophosphorylase (AGP) large subunits from maize, does not reasonably provide enablement for polynucleotides encoding heat stable AGP large subunit mutant enzymes from other plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to polynucleotides encoding any mutant starch biosynthesis protein that is more heat stable than the wild-type protein, a method of increasing heat resistance in a plant via transformation with that polynucleotide, and plants so transformed.

The claims are also drawn to polynucleotides encoding any mutant of any subunit of any AGP and to polynucleotides encoding specific amino acid changes in the large subunit of any AGP.

The instant specification, however, only provides guidance for mutagenesis of maize ADP-glucose pyrophosphorylase (AGP) and selection for heat-stable variants (example 1-2), isolation of the mutant proteins from transformed E. coli and kinetic analysis (examples 3-4), general guidance for pyramiding mutations (example 5), mutation of amino acid 333 to all nineteen other amino acids (tyr, phe and met) to identify three amino acid substitutions that resulted in increased heat stability (example 6), combining the Amino acid 33 mutations with the Rev6 mutation (example 7), and identification of temperature sensitive mutations in AGP (example 9).

The instant specification fails to provide guidance for construction of heat stable mutant AGP large subunits from any plant other than maize.

AGP enzymes from different plants have different lengths and sequences, and so none except the maize enzyme would possess the specified wild type amino acid at the positions specified in claims 6-21 and 32-35. For example, the alanine in bold in Figure 5A of the instant specification is located at amino acid 177 in the maize large subunit AGP, amino acid 183 in the wheat large subunit AGP, amino acid 184 in the barley large subunit AGP, and amino acid 179 in the rice large subunit AGP (Bhave et al, GenBank Accession No. P55241; Ainsworth et al, GenBank Accession No. S60572, Villand et al, GenBank Accession No. P30524; and Satozawa et al, GenBank Accession No. T02965). None of the enzymes form these other plants have a histidine at amino acid 333, and it is not clear that mutating the amino acid that is present at position 333 would result in heat stable enzymes.

Additionally, Table 3 shows that the $His^{333} \rightarrow Gly^{333}$ mutation in maize actually results in a less heat stable enzyme that the wild-type enzyme. Thus, transformation of a plant with an AGP mutant gene comprising such a mutation could not increase the heat stability of the plant.

Lastly, the transformation of whole plants with genes encoding altered plant AGP subunits for increased heat resistance is unpredictable. Lafta et al (1995, Plant Physiol. 109:637-643) teach that in potato there is a lack of relationship between enzyme stability and heat resistance in the whole plant (pg 641, right column, last paragraph to pg 642, left column, 1st full paragraph). Greene et al (1998b, Proc. Natl. Acad. Sci. USA 95:13342-13347) teach that in wheat, starch synthase is responsible for heat-induced seed weight loss (pg 13342, right column, 1st full paragraph). Additionally, transgenic plants containing AGP genes behave unpredictably in other ways. Sweetlove et al (1996, Biochem. J. 320:493-498) found no differences in starch content, tuber number, tuber weight, or metabolite content between potatoes transformed with a gene encoding AGP and control plants, even though the activity of the enzyme was four-fold higher in the transformed plants (pg 495, entire pg, and pg 497, right column, paragraph 3).

As the specification does not describe the transformation of any plant with a gene encoding the heat stable AGP large subunits, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with increased heat stability, if such plants are even obtainable.

10. Claims 1, 3, 5-26 and 29-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules from any plant and encoding heat stable AGP subunits. In contrast, the specification only describes maize AGP large subunit genes that are mutant at a few amino acids. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that encode heat stable AGP subunits within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1, 3, 5-26 and 29-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1 is indefinite in its recitation of "biologically-active fragment". It is not clear what the biological activity of the fragment is - is it the same as the mutant polypeptide or is it some other biological activity?

Claims 5 and 11-13 are indefinite in their recitation of "amino acid corresponding to position(s)" in lines 2-3. It is unclear what it means for an amino acid to correspond to a position.

Claims 6-8 and 31-33 lack antecedent basis for the limitation "said amino acid substituted for ... 333" in lines 1-2

Claims 11-13 and 34-36 lack antecedent basis for the limitation "the native AGP enzyme subunit" in line 4. It is also noted that the phrase makes no sense in the context of the claim.

Claims 19, 25 and 41 are indefinite in their recitation of "dicotyledonous plant is ... prairie grass" as grasses are not dicots.

Claim 29 lacks antecedent basis for the limitation "said polynucleotide molecule" in line 4.

It is not clear if claims 30-36 are directed to a mutant ADP-encoding nucleic acid from maize, while claims 5-8 and 11-13 are directed to a mutant ADP-encoding nucleic acid from any plant, if claims 30-36 are only directed to mutant ADP-encoding nucleic acid from a plant that normally has histidine at position 333, or if claims 30-36 are duplicates of claims 5-8 and 11-13.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 1 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ballicora et al (1995, Plant Physiol. 109:245-251).

Ballicora et al teach a mutation in the small subunit of potato AGP that results in an enzyme with increased heat stability (pg 248, right column).

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1, 3, 5, 30 and 37-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1of U.S. Patent No. 6,069,300. Although the conflicting claims are not identical, they are not patentably distinct from each other because a nucleic acid encoding a maize large AGP subunit mutant with a His^{333} $\rightarrow$ Tyr^{333} mutation, as claimed in the issued patent, is a species of the genus of nucleic acids encoding a maize large AGP subunit mutant with a mutation in His^{333} that confers increased heat stability, as claimed in the instant application.

17. Claims 1, 3, 5, 15-17, 20-23, 26, 30 and 37-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 21-30 and 48-54 of U.S. Patent No. 6,403,863. Although the conflicting claims are not identical, they are not patentably distinct from each other because nucleic acids encoding maize large AGP subunit mutants, including ones with substitutions of His^{333} $\rightarrow$ an amino acid that confers increased heat stability and His^{333} $\rightarrow$ Tyr^{333}, a method for using the nucleic acid to increase heat resistance in a plant, including in maize, wheat, rice, and barley, and plants, plant tissues and seeds so obtained, as claimed in the issued patent, is a species of the genus of nucleic acids encoding a maize large AGP subunit mutant with a mutation in His^{333} that confers increased heat stability, a method for using the nucleic acid to increase heat resistance in a plant, including in maize, wheat, rice, and barley, and plants, plant tissues and seeds so obtained, as claimed in the instant application.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
July 24, 2003